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## INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

<b>(51) International Patent Classification <sup>5</sup> :</b> <b>G01N 33/15, A61K 31/54, C07D 279/18, B65D 69/00, 71/00</b>	<b>A1</b>	<b>(11) International Publication Number:</b> <b>WO 94/16325</b> <b>(43) International Publication Date:</b> 21 July 1994 (21.07.94)
<b>(21) International Application Number:</b> PCT/US93/00352 <b>(22) International Filing Date:</b> 14 January 1993 (14.01.93) <b>(71) Applicant (for all designated States except US):</b> CTM ASSOCIATES, INC. [US/US]; P.O. Box 599, Washington Crossing, PA 18977 (US). <b>(72) Inventor; and</b> <b>(75) Inventor/Applicant (for US only):</b> CIPRIANI, Pier, J. [US/US]; 285 Sentinel Avenue, Newtown, PA 18940 (US). <b>(74) Agent:</b> DRUMMOND, William, H.; Suite 500, 4590 MacArthur Boulevard, Newport Beach, CA 92660 (US).		<b>(81) Designated States:</b> AU, CA, JP, KR, RU, US, European patent (AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).  <b>Published</b> <i>With international search report.</i>
<b>(54) Title:</b> METHOD AND KIT FOR EPITHELIAL CANCER SCREENING  <b>(57) Abstract</b>  A diagnostic kit and method for performing routine screening procedures to detect possible epithelial cancer. The kit includes prepackaged reagents, containing preselected volumes at preselected concentrations to permit direct dispensation of each of the reagents directly from its package without further mixing or measuring steps.		

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METHOD AND KIT FOR EPITHELIAL CANCER SCREENING

5 This invention relates to improved methods of screening patients for epithelial cancer.

10 In another respect, the invention relates to a kit for use in screening patients to detect possible epithelial cancer.

More particularly, the invention pertains to a kit for use in screening patients for epithelial cancer, which can be used by medical personnel without highly specialized training.

15 In yet another respect, the invention pertains to a kit for use in screening patients for epithelial cancer, which places all of the necessary materials in "ready-to-use" form at the immediate disposal of clinical personnel, without requiring time-consuming or complicated mixing-storage-dispensing-measuring steps.

20 Various procedures are known for screening patients for epithelial cancer, especially for detecting suspected cancerous and precancerous sites on the mucosa such as the oral mucosa. Such procedures generally employ a dye which preferentially stains RNA-rich tissues, which have been recognized as characteristic of cancerous and precancerous conditions. For example, the U.S. patent to Mashberg No. 4,321,251 discloses such a procedure. The procedure of

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Mashberg involves sequential washes, rinses and applications of water, diluted acetic acid and a solution of toluidine blue-O dye in the mouth to detect cancerous and precancerous conditions of the oral mucosa. This wash-rinse-application-  
5      rinse-wash procedure is then repeated when a suspected site is detected, to reduce the number of false positives.

It would be highly advantageous to screen all patients for epithelial cancer during routine office visits, such as  
10      visits to dental offices for teeth cleaning, etc. However, methods of screening for epithelial cancer such as the Mashberg procedure have not achieved routine use, partly because the mixing, measuring and dispensing the solutions required is too time consuming to be done for each patient by  
15      the dentist and such procedures require some training and experience beyond that normally possessed by para-professional assistants.

It would therefore be desirable to provide an improved  
20      method for screening patients for epithelial cancer which is simplified and especially adapted to promote routine screening as the adjunct to normal visits by the patient to medical or dental offices for other reasons.

25      Accordingly, the principal object of the present invention is to provide such improved screening methods.

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Yet another object of the invention is to provide apparatus which encourages such routine testing, by minimizing the time and complications which formerly discouraged such routine testing by medical and dental professionals.

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These and other, further and more specific objects and advantages of the present invention will be apparent to those skilled in the art from the following detailed description thereof, taken in conjunction with the drawing, which depicts a kit of components assembled in accordance with the principles of one embodiment of the invention.

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Briefly, in accordance with the invention, I provide methods and apparatus for screening patients for epithelial cancer.

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My method is an improvement of prior art screening methods which include the steps of sequentially applying to suspected cancerous or precancerous sites preselected volumes of at least two liquid testing reagents of preselected concentrations. My improved method comprises providing such reagents to the administering clinician in prepackaged form, each of said reagents be packaged to contain the preselected volume thereof at the preselected concentration thereof, to permit direct dispensation of each such reagent directly from its package for use in accordance with the screening procedure, without further mixing or measuring steps.

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In accordance with another embodiment of the invention I provide a diagnostic kit for performing routine screening procedures to detect possible epithelial cancer. Such procedures include the steps of sequentially applying  
5 preselected volumes of at least two testing reagents of preselected concentrations to suspected cancerous or precancerous sites. The kit includes a separate package of each of the testing reagents. Each of the packages contains the preselected volume of the reagent in the preselected  
10 concentration thereof.

The drawing depicts a kit constructed in accordance with the principles of the invention, in this case for carrying out the Mashberg screening procedure. The kit can is conveniently  
15 contained in a single box 10 which contains all of the components necessary for screening a single patient for oral epithelial cancer. The components include three bottles 11, 12 and 13, with single use cups. Bottle 11 contains 10cc of a pre-rinse solution which is a 1% solution of acetic acid,  
20 used to adjust the Ph of the oral cavity and wash away food particles and the like. Bottle 12 contains 10 cc. of a 1% solution of toluidine blue-O. Bottle 13 contains 30 cc. of 1% acetic acid solution post-rinse, which is used to remove excess toluidine blue-O dye from the mouth. In accordance  
25 with the presently preferred embodiment, I also include other optional components in the kit such as an oral diagram sheet 14, on which the clinician can record the location of any suspected cancerous sites for later reference, a patient bib

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15, cups 16 for administering water washes and a clinical information reply card 17 which is used to confirm the effectiveness of the procedure.

5           As will be apparent to those skilled in the art, my invention is not limited to a specific treatment method or specific solutions. Instead, it is generally applicable to any epithelial cancer detection procedures which employ a plurality of testing reagents, without limitation on the  
10           specific testing reagents employed.

          Having described my invention in such terms as to enable those skilled in the art to understand and practice it, and having identified the presently preferred embodiments thereof,  
15           I CLAIM:

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## Claims:

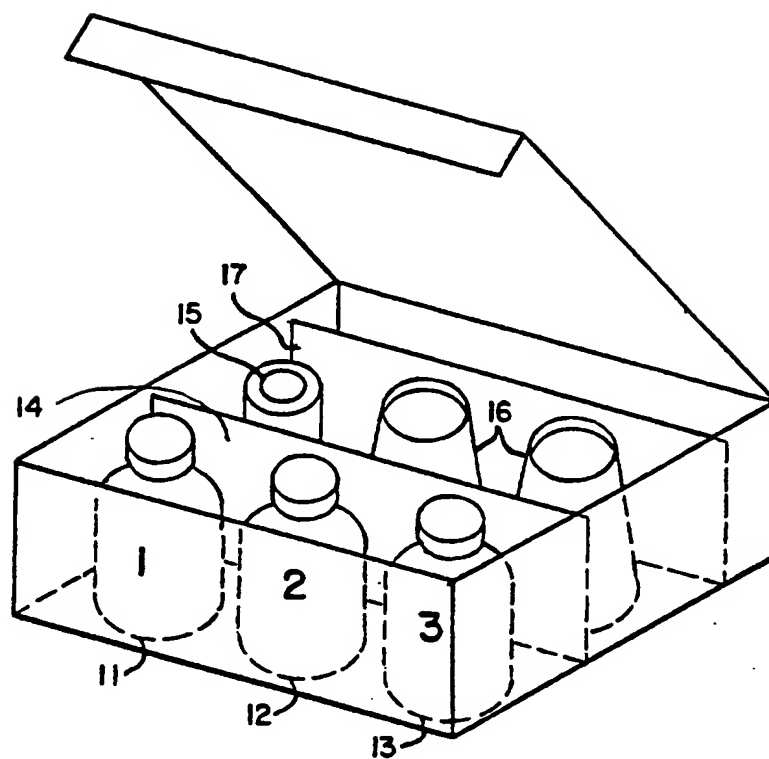
1. In a method for screening patients for epithelial cancer, according to a procedure which includes steps of sequentially applying to suspected cancerous or precancerous sites preselected volumes of at least two liquid testing reagents of preselected concentrations, the improvement comprising providing such reagents to the administering clinician in prepackaged form, each of said reagents being packaged to contain the preselected volume thereof at the preselected concentration thereof, to permit direct dispensation of each such reagent directly from its package for use in accordance with the screening procedure, without further mixing or measuring steps.



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2. A diagnostic kit for performing routine screening procedures to detect possible epithelial cancer, said procedures including the steps of sequentially applying to suspected cancerous or precancerous sites, preselected volumes of at least two testing reagents of preselected concentrations, said kit including a separate package of each of said testing reagents, each said package containing said preselected volume said reagent in the preselected concentration thereof.

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*FIG. 1*

## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US93/00352**A. CLASSIFICATION OF SUBJECT MATTER**

IPC(5) :G01N 33/15; A61K 31/54; C07D 279/18; B65D 69/00,71/00

US CL :424/7.1.9; 514/226.2; 544/37; 206/569

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)

U.S. :

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched  
"REMINGTON'S PHARMACEUTICAL SCIENCES" AND "THE PHYSICIANS DESK REFERENCE"

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

APS &amp; STN [TOLUIDINE BLUE(INCLUDING RESISTRATION#)] AND ((ORAL OR TONGUE OR MOUTH OR GUMS)(2A)(CANCER OR SARCOMA))

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US, A, 4,321,251 (MASHBERG), 23 March 1982, See col. 2, lines 15-35.	1 & 2
Y	N, REMINGTON'S PHARMACEUTICAL SCIENCES, issued 1975, (HOOVER, JOHN E.) pages 1368, 1369 & 1413-1418.	1,2
A	US, A, 4,977,177 (BOMMER ET AL.) 11 December 1990, See col. 12, lines 8-45.	1,2
Y	US, A, 5,018,531 (HARTMAN) 28 May 1991, See abstract.	1,2
Y	US, A, 3,743,088 (HENKIN) 03 July 1973, See abstract.	1,2

☐ Further documents are listed in the continuation of Box C.☐ See patent family annex.

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Date of the actual completion of the international search

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